Galatea of the Microbes:

Biological Identity as a Composite Reality

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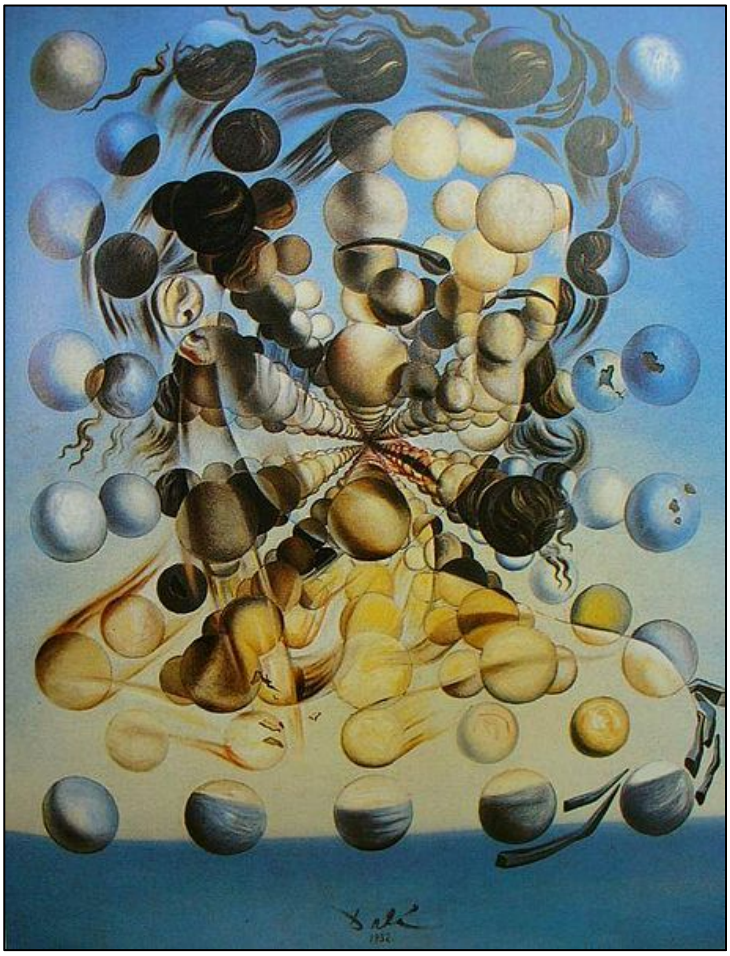

I am a "we". Indeed, each human being, like every living thing, is a composite reality, made up of many heterogeneous living constituents, belonging to different species, and even to different kingdoms. Each living thing looks a bit like Dalí's painting *Galatea of the Spheres*. At a distance, you see the graceful (though disquieting) face of Gala, Dalí's wife and muse; but as you get closer, you start to realize that Gala is in fact made up of a multitude of small spheres, as if the very unity of Gala was the provisory coming together of a myriad of atoms. The same is true of living things, though perhaps *Galatea of the Microbes* would be a more appropriate name.

For instance, you, a reader of *The Philosophers' Magazine*, are made of 90% of bacteria, and only 10% of (classically conceived) "human" cells. Those bacteria live in many of your organs – like your mouth, lungs, sexual organs and gut. And it is not just bacteria. In and on you live also many fungi and viruses. As a whole, a human being hosts around 100 trillion symbiotic microbes (the "microbiota"). What is both scientifically and philosophically fascinating is that the examination of what these tiny aliens do in our bodies leads us to a radical re-interpretation of what our very identity is.

When we hear about microbes, our first reaction is usually to back away. One of the greatest advances in modern medicine has been the realization that many diseases are due to pathogens, in particular bacteria and viruses. The "germ theory of disease", often associated with the great figures of Robert Koch and Louis Pasteur, has had a great influence on the way we conceive of our health and the best way to preserve it. Pathogenic microbes, however, constitute only a tiny minority of the microbes with which we interact. Microbes are everywhere around us, on us and in us. They have been on earth for more than 3.5 billion years, and they will certainly still be there long after the human species disappears. Bacterial biomass certainly outweighs the biomass of all animals and plants taken together. The world has been and still is mainly microbial, to the extent that all plants and animals can, perhaps, be seen to be nothing more than biological epiphenomena (though interesting ones, of course – at least to our own eyes).

But what does it mean to say that *we* are, to a large degree, "microbial"? Each human being hosts a unique collection of microbes, with the greatest quantities found in the gut, in particular in the colon (around 10^{12} bacteria). From a cellular point of view, a "human" is 90% bacterial, but from a genetic point of view, it is 99% bacterial. These microbes are not just "passengers" in our bodies; many of them play key functional roles in us, and in most cases our interactions with them are "mutualistic". By "mutualism", evolutionists mean an interaction that benefits (that is, increases the fitness of) both partners. Some of our tissues, as our gut for instance, constitute an extraordinarily rich niche for bacteria, a place where they can easily feed and reproduce. Reciprocally, research done in the last fifteen years or so has demonstrated that some bacteria are indispensable to realize essential functions of the body. It has been known for decades that certain bacteria are indispensable for digestion in many organisms, including mammals. Recently, though, the concept of what microbes can do in their hosts has changed dramatically. In mice, mutualistic bacteria have been proved indispensable for normal development (especially of the gut-associated lymphoid tissue), and for immune defence and homeostasis. But when exactly do these bacteria first become part of our living systems? For a long time, it has been thought that the foetus was growing in a sterile intrauterine environment, and that our colonization by bacteria started at birth. But it has been shown this year that our interactions with microbes start even before birth (Aagaard et al., "The Placenta Harbors a Unique Microbiome", 2014). So, almost from the moment of conception, microbes are involved in our growth and development.

Bacteria could even impact dramatically host behaviours, in particular the level of stress. Several research teams are currently investigating the possible role of abnormal microbiota in the development of neurological disorders such as autism. As explained by Sekirov and colleagues ("Gut Microbiota in Health and Disease", 2010), disruptions in the normal microbiota may lead to colonization by autism-triggering microbes, or to the overgrowth of some specific bacteria that produce neurotoxins. Antimicrobial therapy is often associated with the onset of autism, and gastrointestinal abnormalities are often found in autistic patients. Nevertheless, more research is naturally needed on this question, all the more so as it is particularly sensitive in our societies.

Importantly, the influence of microbes on host physiology extends well beyond the case of mammals. This phenomenon is well documented in insects, squids, sponges, leguminous plants, and more. A fascinating and now very well known example is that of the squid *Euprymna scolopes*. This tiny aquatic creature found near Hawaii hunts at night, and uses a "light organ" to hide its own shadow to potential predators. Margaret McFall-Ngai and colleagues have shown that the organogenesis of this essential light organ depends on the colonization of the squid by one specific bacterium, *Vibrio fischeri*, a bacterium that the squid actively recruits, while it voids itself of all other bacteria. The whole physiology of the developing squid, from its "harvesting" system to its immune system, insures the successful recruitment of this particular bacterium, which makes the full development of the squid possible. As shown by Gilbert and Epel in their book *Ecological Developmental Biology* (2009), symbiotic interactions, long thought as intriguing exceptions, are in fact close to the rule in nature Even microbes themselves are heterogeneous entities: bacteria and archaea contain many viruses ("bacteriophages"), many of which seem to contribute critically to their functioning. And even viruses are now known to host "virophages" (very small entities that reproduce within viruses – often, but not always, in a pathogenic way)! Consequently, the kind of biological integration described here is extremely general in nature, and this is a point we should keep in mind, even for those of us who are, understandably, interested first and foremost in unravelling our identity as human beings. Each living thing is "heterogeneous", meaning here, quite specifically, that it is made of a huge number of entities belonging to different species.

Collectively, the examples examined above show that the microbiota is indispensable for the functioning, development and preservation of living things. Therefore, the microbiota constitutes a real "organ" of the body, and indeed one of the most indispensable of all organs.

The consequence of all this is that biological identity is always a composite, "impure", identity. Both folk wisdom and biological science of a recent past suggest that an organism is homogenous, autonomous and "self-defined". Jacques Monod, for instance, wrote in *Chance and Necessity* that a living being exhibits "an autonomous determinism: precise, rigorous, implying virtually total 'freedom' with respect to outside agents or conditions". And for François Jacob in *The Possible and the Actual*: "The chromosomes of a fertilized egg contain, written in the DNA, the plans that direct the development of the future organism, its activities, its behavior." Many people today still believe that what we are is dictated to a large extent by our genes, that a living thing is the product of the unfolding of "instructions" contained in those genes, and that this living thing defends itself against any "foreign" threat. We now know that this view of our biological identity, and of the way it is constructed through time, is utterly wrong. A living thing is constructed in a complex way through the interactions of many different entities – including genes, regulatory proteins, and the environment. And elements long thought to be part of the "external environment", such as mutualistic bacteria, are now increasingly recognized as true constituents of the body. The building and persistence of a living thing presupposes the controlled integration of genetically "foreign" elements, far from being based on the preservation of a genetically defined identity. It is still possible to define the "inside" and the "outside" of a living thing (though these boundaries, like all biological boundaries, are likely to be fuzzy), but it would be entirely inappropriate to think that only constituents "coming from the inside" of a living thing can be *part* of this living thing. Recently, Gilbert, Sapp and Tauber have even suggested that current data on symbiosis suggests that "we have never been individuals". In my view, the ubiquity of symbiotic interactions puts into question not so much the concept of individuality as such, but rather one influential conception of individuality, namely the idea that an individual would be a self-defined and autonomous entity.

Yet the realization of the fantastic plurality and diversity of constituents of every living thing is certainly not the end of the story. Some living things exhibit a high degree of unity and organization, and for that reason they are more appropriately described as "organisms". An organism is not just a *collection* or *community* of constituents. The constant activity of an organism is *to unify this plurality of constituents*. This is the moment when we step back, and see that Galatea of the Spheres is also, after all, *one* woman, namely Gala: clearly emerging from the slightly upsetting diversity of the small spheres, there is Gala, a human being who is certainly different from what we had thought at first sight (before seeing the spheres of which she is constituted) but who nonetheless expresses a high degree of unity. In other words, as I see it, we should recognise three steps in our thoughts about biological identity: first, we see apparent unity (we think that we know that this a just a portrait of a woman; by analogy, we think that we know what an organism is); second step, this vision is exploded (we realize that, in fact, Gala bursts into a myriad of spheres; by analogy, we realize that an organism like us is in fact the nexus of trillions of interacting entities); third step, we reunite the disparate parts (we figure out that what we have under our eyes is not just *any* collection of spheres, it is a very peculiar association of heterogeneous spheres which, in the end, constitutes what Gala is; by analogy, we figure out that an organism is precisely the constant unification of heterogeneous constituents, a unification which, ultimately, gives to the organism its high degree of unity).

In a nutshell, what all this shows is that there is no tension between being plural and being one: an organism is the continuous creation of the unity of a plurality. But what are exactly the biological processes that ensure that an organism is indeed a unit? There are certainly many of them, interacting one with the other, but in my research, and in particular in my book *The Limits of the Self: Immunology and Biological Identity*, I have insisted on the central role played by one of them: the immune system. The immune system offers an inclusion/exclusion principle: it plays a crucial role in determining what is a part of an organism and what is not, by constantly accepting or rejecting entities. This principle is not based on an endogenous vs. exogenous distinction: many genetically foreign entities (for example, mutualistic bacteria in the gut) are tolerated, while some genetically endogenous entities can be eliminated (for example, dead cells engulfed by macrophages). This is why I think that the old vocabulary of self vs. nonself, which has dominated immunology since the 1940s, must now be considered as inadequate. The immune system is not a system of detection and elimination of what is "foreign" to the organism. It plays a key role in the definition of the boundaries of the organism, but not on the basis of the origin of the constituents with which it interacts. Thus, in my view at least, the immune system is critical for the constant re-definition of what belongs and what does not belong to an organism, and therefore for the constant re-definition of the organism's identity through time ("diachronic" identity). Importantly, this conception applies very broadly to the living world, as recent research has shown that immune systems are found in insects, plants and even prokaryotes.

The setting up of a novel conception of biological identity, which takes into account ongoing scientific research, can only be made via the collaboration of philosophers and scientists. The dialogue between science and philosophy is today as indispensable as ever. With distinguished immunologists, we suggested a novel theoretical framework to better account for the triggering of an immune response, and this research has been published in several scientific journals (see, in particular, Pradeu, Jaeger and Vivier, "The Speed of Change: Towards a Discontinuity Theory of Immunity?", 2013). This framework, called the "discontinuity theory", submits that immune responses are not due to the presence of "foreign" entities in the body, but to sudden modifications in the organism (regardless of their endogenous or exogenous origin). The discontinuity theory, in particular, helps to shed light on how the organism tolerates huge quantities of mutualistic microbes.

The view of the organism as the constant unification of a plurality of heterogeneous biological constituents naturally has consequences for philosophical discussions about what makes our identity as human beings. Several philosophers, including Eric T. Olson, have defended the "biological approach" to human identity, according to which a human being is the same through time if and only if there exists a biological continuity – a metabolic continuity – between her different states (in contrast, in particular, with the "psychological view", which states that a human being is the same through time if and only if there exists a psychological continuity – consciousness, thoughts, memories – between her different states). There is much to be said in favour of the biological approach. And yet when Olson equates being a metabolic part of an organism with being the product of the realization of a plan encoded in its genes (*The Human Animal*, 1997, p. 135), it should be clear that this view, which was perhaps acceptable in 1997, must now be rejected. (This does not go against the biological approach as such; rather, it shows, quite unsurprisingly, that if this approach is to be both fruitful and precise, it will be only by being revised regularly on the basis of ongoing scientific research).

Now what does the conception of biological identity as a composite reality change in our everyday lives? In fact, the view defended here has many practical consequences, including medical ones. A patient should be seen as *this* human being, *its microbiota included*. The microbiota can influence pathological states such as obesity, inflammatory bowel disease, neurodevelopmental disorders, or cancers. To design efficient treatments, it is very important to take the microbiota into account (see for instance Pennisi, "Cancer therapies use a little help from microbial friends", 2013). Moreover, if resident bacteria are seen to be parts of us, one may think we would do well to use antibiotics considerately. It can even be good to establish or restore an appropriate microbiota, for instance through the use of probiotics, that is, through the administration of microorganisms known for their beneficial effects. Another important example concerns fecal microbiota transplantation, the infusion of donor feces in a sick patient.

Recent studies have shown that this therapeutic strategy, first suggested more than fifty years ago, was extremely successful (Kelly, "Fecal Microbiota Transplantation – An Old Therapy Comes of Age", 2013). Another application, probably more appealing than the last, relates to forensic science: some of our bacteria, skin bacteria in particular, are so unique to each of us that they can be a very efficient way to identify us, complementing DNA-based forensic methods.

A new and very exciting view of what it means to be *one* organism is emerging from current biological sciences. To be "one" is certainly not inconsistent with being "plural"; in fact, the unity of an organism results from a continuous biological work, which consists in the constant unification of heterogeneous constituents. Coming back to Dalí, we could say that the microbial spheres are part of a continuously activated and integrating network, which gives Gala her biological unity.